of the claim [sic] invention or to enable one skilled in the art to make and use the claimed invention for those reasons of record in Paper No. 6." According to the rejection, the production of the claimed protein requires an isolate nucleic acid for which there is no adequate written description in the specification. In the Examiner's view, the "fact that the instant specification discloses a method through which that nucleic acid might or might not be isolated is irrelevant . . . because it is the isolated nucleic acid, not the method of isolating the nucleic acid, which is required to produce and define the claimed protein." In support of this conclusion, the Office Action cites *Amgen, Inc. v. Chugai Pharmaceuticals Co. Ltd.*, 18 USPQ2d, at 1016. Applicants were further encouraged to review the recent CAFC decision in *The Regents of the University of California v. Eli Lilly and Company*, 43 USPQ2d 1398.

Applicants disagree, and respectfully traverse the rejection.

***1. Proper Legal Standard***

The statute

35 U.S.C. §112 provides in pertinent part that:

"*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same . . .* "

Relevant case law

For the Examiner's convenience, copies of the decisions cited in the following analysis of relevant case law, with the exception of *Amgen v. Chugai*, and *U.C. v. Lilly* which were cited by the Examiner, are submitted along with the present reply.

The function of the "written description" requirement in §112 is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific invention later claimed by him. Accordingly, the test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed, would reasonably have conveyed to a person of ordinary skill in the pertinent art that the inventor had possession at that time of the later claimed subject matter. *In re Kaslow*, 217 USPQ 1089, 1096 (Fed. Cir. 1983). In determining compliance with the written description requirement, each case must be decided on its own specific facts, taking into account the nature of the invention and the amount of knowledge imported by the disclosure to those skilled in the art. *Application of Driscoll,* 195 USPQ 434 (CCPA 1977), at 436-438; *Application of Wertheim*, 191 USPQ 90 (CCPA 1976), at 96-97; *Ralston v. Purina*, 222 USPQ 863 (D.C. D. Kansas, 1984), at 896.

In *Amgen v. Chugai, supra*, the relevant claim read as follows:

"*A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.*"

The CAFC has held that a "gene is a chemical compound, albeit a complex one", and its conception does not occur "unless one has a mental picture of the structure of the chemical, **or is able to define it by its method of preparation**, its physical or chemical properties, or whatever characteristics sufficiently distinguish it." *Amgen*, 18 USPQ, at 1021, emphasis added. This

language implies, consistent with prior case law, that knowledge of the actual sequence is not an absolute requirement for conception, provided that the inventor discloses an enabling means to obtain the DNA.

In *Fiers v. Sugano*, 25 USPQ 1601 (1993), the CAFC again considered conception of an invention defined in a single count reading as follows:

> "*A DNA which consists essentially of a DNA which codes for a human fibroblast interferon-beta polypeptide.*"

Fiers was filed on April 3, 1981 and sought priority of its British application filed on April 3, 1980. Citing *Amgen*, Fiers argued that *Amgen* held that a conception of a DNA can occur in the absence of a disclosure of the sequence of the claimed DNA, provided that an enabling method is disclosed for the preparation of the DNA. Although the CAFC rejected this argument with regard to the above count, it noted that

> "*Our statement in Amgen that conception may occur, inter alia, when one is able to define a chemical by its method of preparation requires that* ***the DNA be claimed by its method of preparation***. ***We recognize that, in addition to being claimable by structure or physical properties, a chemical material can be claimed by means of a process***. *A product-by-process claim normally is an after-the-fact definition, used after one has obtained a material by a particular process. Before reduction to practice,* ***conception only of a process for making a substance****, without conception of a structural or equivalent definition of that substance,* ***can*** *at most* ***constitute a conception of the substance claimed as a process***. *Conception of a substance* ***claimed per se*** *without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties.*"

*Fiers, supra*, at 1604-1605, emphasis added.

Accordingly, *Fiers*, at least *in dictum*, acknowledges the possibility that the conception of a process for making a substance can constitute a conception of the substance itself claimed as a process, i.e. in a product-by-process format.

In *University of California v. Eli Lilly, supra*, the claim considered by the CAFC read as follows:

> "*A DNA transfer vector comprising a deoxynucleotide sequence coding for human proinsulin, the plus strand of said cDNA having a defined 5' end, said 5' end being the first deoxynucleotide sequence coding for human proinsulin.*"

*University of California, supra,* at 1401.

With regard to this **product claim**, which covers a vector DNA including the coding sequence of human proinsulin, the CAFC read *Fiers* to dictate that

> "*an adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, 'requires a precise definition, such as by structure, formula, chemical name, or physical properties,' not a mere wish or plan for obtaining the claimed chemical invention.*"

*University of California, supra*, at 1404.

This decision does not affect the acknowledgment in *Fiers* that the conception of a process for making a substance can constitute a valid conception of the substance claimed as a "product-by-process."

Acceptance of product-by-process claims began over a century ago, in *Ex parte Painter*, 1891 C.D. 200 (Comm'r of Pats. 1891). Product-by-process claims were initially granted only when the invention could not otherwise be defined ("the necessity rule"). However, the necessity rule is no longer applied rigidly, rather product-by-process claims are held proper whenever the requirements of Section 112 are satisfied, provided that other requirements of patentability are also met. *In re Moeller*, 48 USPQ 542, 1941 C.D.; *In re Luck*, 177 USPQ 523 (CCPA 1973); *In re Steppan*, 156 USPQ 143 (CCPA 1967); *In re Pilkington*, 162 USPQ 145 (CCPA 1969).

**2. *The Specification Provides the Legally Required Written Description for Claims 31 to 33.***

Claims 31 to 33 pending in the present application are product-by-process claims, i.e. claims defining a product in terms of the process by which it is made. Such claims are proper under governing case law, as acknowledged in MPEP §2173.05(p).

Whether in any given case the written description requirement is met, is decided by a case-by-case determination, taking into account the nature of the invention and the amount of knowledge imported by the disclosure to those skilled in the art. Accordingly, each case must be determined on its own facts, in view of the general state of the art, and the knowledge of an ordinary person skilled in the art.

In Paper No. 6, the Examiner acknowledged that "[t]he instant specification describes the isolation of cDNAs encoding two TNF receptor associated factor (TRAF) proteins of murine origin

and the isolation of the proteins encoded thereby. It also contains ample suggestions that homologous human proteins could be isolated by employing those methods that are routine in the art of molecular biology." However, in the current Office Action, the Examiner labeled all this teaching "irrelevant", maintaining that, even though the claims pending are product-by-process claims, under the *Amgen* decision, "it is the isolated nucleic acid, not the method of isolating the nucleic acid, which is required to produce and define the claimed protein."

This reading of *Amgen* is believed to be clearly erroneous.

Both *Amgen* and *Fiers* explicitly leave open the possibility of relying on the conception of a process as a date of conception for a product claimed in the form of a product-by-process claim. In other words, under these decisions, an enabling description of a process for making a product claimed in terms of its process of making can satisfy the written description requirement of 35 U.S.C. §112, first paragraph. This particular issue is not specifically addressed in the *U.S. v. Lilly* decision, which, therefore, does not alter the outcome. Accordingly, contrary to the Examiner's view, the question to be decided is whether the present application provides an enabling disclosure for the process described in the pending claims. As the existence of such an enabling disclosure for the process of making human TRAF proteins is acknowledged in Paper No. 6, the rejection of Claims 31 to 33 under 35 U.S.C. §112, first paragraph is improper and should be withdrawn.

It is additionally noted that *Amgen* dealt with issues of conception as of 1981. Similarly, the *Fiers* patent application was filed in 1981 and sought priority based on prior conception coupled with diligence based on a British application filed a year before. In contrast, the present application claims the priority of parent application Serial No. 08/250,858, filed on May 27, 1994, about thirteen years after the *Amgen* and *Fiers* applications. During these thirteen years, recombinant DNA technology has shown a tremendous advance. For example, techniques like PCR amplification, two-hybrid method, advanced techniques of chemical synthesis for DNA were not available in the early

1980's but have become routine laboratory procedures by 1994. Therefore, even if the holdings of *Amgen* and *Fiers* would be directly applicable, as they are not, to the extent that they are based on factual findings concerning the state of the art in the early 1980's, they cannot be applied indiscriminately to the instant application.

Finally, the Examiner's remark in Paper No. 6 that in view of the relatively low homology between the murine and human TNF-R1 receptors a skilled artisan "would not reasonably expect the proteins associated therewith to be conserved between mice and humans" should have of no bearing on the existence or non-existence of adequate written description in the present application for a method of making a human TRAF protein. As noted before, the test is whether the disclosure of the application as originally filed, would reasonably have conveyed to a person of ordinary skill in the pertinent art that the inventor had possession at that time of the later claimed subject matter. The present specification is clear in its disclosure that the human protein can be obtained, for example, by expression of a DNA isolated from a human recombinant cDNA library expressing human TNF-R2 by the yeast two-hybrid technique or by hybridization with a murine TRAF1 or TRAF2 DNA. Accordingly, a skilled artisan, reading the specification of the present application, would have had no doubt that the inventors intended these methods to be part of their invention. The Examiner provided no evidence that the disclosed methods do not work for obtaining and expressing the human TRAF sequence. Indeed, the murine and human TRAF proteins show an 86% overall sequence identity, which makes the cross-species hybridization approach clearly applicable.

In view of the foregoing arguments, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

## II.

## REJECTION UNDER 37 U.S.C. § 112, SECOND PARAGRAPH

Claims 31 to 33 were rejected under 35 U.S.C. §112, second paragraph as "being indefinite."

(a) Claims 31 to 33 were held "indefinite" in their usage of the term "about 30 to 50 bases", since, according to the rejection, "one can not distinguish between that which is encompassed by this term and that which is excluded."

The use of the term "about" in patent claims was specifically held acceptable in *Ex parte* Eastwood et al., 163 USPQ 316. Accordingly, the withdrawal of this rejection is respectfully requested.

(b) Claims 31 to 33 were rejected as "vague and indefinite because the instant specification does not identify that material property of [sic] combination of properties which is unique to and, therefore, definitive of a TRAF protein for those reasons of record in Paper Number 6."

Applicants fail to understand this rejection. Claims 31 to 33 were rejected in Paper No. 6 for similar reasons since they contained the limitation "obtainable", which was interpreted as a functional limitation whereas the claims were read as being drawn to a composition of matter. Citing *In re Hutchison*, the Examiner noted that "functional statements contained therein do not limit article claims."

Without acquiescence in the Examiner's position concerning the claims rejected in Paper No. 6, the present claims are product-by-process claims, which are properly characterized by process

steps. Should this rejection be maintained, the Examiner is respectfully requested to explain how it applies to the claims pending in the present application.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Respectfully submitted,
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